

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 98N-0721]

**Agency Information Collection Activities: Proposed Collection; Comment Request;
Premarket Approval of Medical Devices**

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing an opportunity for public comment on the proposed collection of certain information by the agency. Under the Paperwork Reduction Act of 1995 (the PRA), Federal agencies are required to publish notice in the **Federal Register** concerning each proposed reinstatement of an existing information collection of information, and to allow 60 days for public comment in response to the notice. This notice solicits comments on requirements for premarket approval applications (PMA's).

DATES: Submit written comments on the collection of information by *(insert date 60 days after date of publication in the Federal Register)*.

ADDRESSES: Submit written comments on the collection of information to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number found in brackets in the heading of this document.

FOR FURTHER INFORMATION CONTACT: Margaret R. Schlosburg, Office of Information Resources Management (HFA-250), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-1223.

SUPPLEMENTARY INFORMATION: Under the PRA (44 U.S.C. 3501–3520), Federal agencies must obtain approval from the Office of Management and Budget (OMB) for each collection of

information they conduct or sponsor. Collection of information is defined in 44 U.S.C. 3502(3) and 5 CFR 1320.3(c) and includes agency requests or requirements that members of the public submit reports, keep records, or provide information to a third party. Section 3506(c)(2)(A) of the PRA (44 U.S.C. 3506(c)(2)(A)) requires Federal agencies to provide a 60-day notice in the **Federal Register** concerning each proposed collection of information, including each proposed reinstatement of an existing collection of information, before submitting the collection to OMB for approval. To comply with this requirement, FDA is publishing notice of the proposed collection of information listed below.

With respect to the following collection of information, FDA invites comments on: (1) Whether the proposed collection of information is necessary for the proper performance of FDA's functions, including whether the information will have practical utility; (2) the accuracy of FDA's estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used; (3) ways to enhance the quality, utility, and clarity of the information to be collected; and (4) ways to minimize the burden of the collection of information on respondents, including through the use of automated collection techniques, when appropriate, and other forms of information technology.

I. Premarket Approval of Medical Devices—21 CFR Part 814 and FDAMA Sections 201, 202, 205, 207, 208, 209, 216, 217, and 403 (OMB Control Number 0910–0231—Extension)

Section 515 of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 360e) sets forth requirements for premarket approval of certain medical devices. Under section 515 of the act, an application must contain several pieces of information, including: Full reports of all information concerning investigations showing whether the device is safe and effective; a statement of components; a full description of the methods used in, and the facilities and controls used for, the manufacture and processing of the device; and labeling specimens. The implementing regulations, contained in part 814 (21 CFR part 814), further specify the contents of a PMA for a medical device and the criteria FDA will employ in approving, denying, or withdrawing approval

of a PMA. The purpose of these regulations is to establish an efficient and thorough procedure for FDA's review of PMA's for class III (premarket approval) medical devices. The regulations will facilitate the approval of PMA's for devices that have been shown to be safe and effective and otherwise meet the statutory criteria for approval. The regulations will also ensure the disapproval of PMA's for devices that have not been shown to be safe and effective and that do not otherwise meet the statutory criteria for approval.

Under § 814.15, an applicant may submit in support of a PMA studies from research conducted outside the United States, but an applicant must explain in detail any differences between standards used in a study to support the PMA's and those standards found in the Declaration of Helsinki. Section 814.20 provides a list of information required in the PMA, including: A summary of information in the application, a complete description of the device, technical and scientific information, and copies of proposed labeling. Section 814.37 provides requirements for an applicant who seeks to amend a pending PMA. Section 814.82 sets forth postapproval requirements FDA may propose, including periodic reporting on safety effectiveness, and reliability, and display in the labeling and advertising of certain warnings. Other potential post approval requirements include the maintenance of records to trace patients and the organizing and indexing of records into identifiable files to enable FDA to determine whether there is reasonable assurance of the device's continued safety and effectiveness. Section 814.84 specifies the contents of periodic reports.

II. FDA Modernization Act of 1997

The Food and Drug Administration Modernization Act of 1997 (FDAMA), enacted on November 21, 1997, to implement revisions to the act, streamlines the process of bringing safe and effective drugs, medical devices, and other therapies to the U.S. market. Several provisions of this act which affect the PMA process and impact collection of information have been or will be implemented by FDA and are discussed as follows.

Section 201(b) of FDAMA amends section 515(d) of the act to allow submission of data from investigations of earlier versions of a device, in support of a safety and effectiveness

determination for a PMA. The data is valid if modifications to earlier versions of the investigational device, whether made during or after the investigation, do not constitute a significant change that would invalidate the relevance of the data. This section also allows for the submission of data or information relating to an approved device that are relevant to the design and intended use of a device for which an application is pending, provided the data are available for use under the act (i.e., available by right of reference or in the public domain).

Section 202 of FDAMA amends section 515(d) of the act to state that FDA will provide special review, which can include expedited processing of a PMA application, for certain devices intended to treat or diagnose life threatening or irreversibly debilitating diseases or conditions.

Section 205(a) of FDAMA amends section 513(a)(3) of the act to allow sponsors planning to submit a PMA to submit a written request to FDA for a meeting to determine the type of information (valid scientific evidence) necessary to support the effectiveness of their device. FDA must meet with the requester and communicate in writing the agency's determination of the type of data that will be necessary to demonstrate effectiveness within 30 days after the meeting.

Section 205(c) of FDAMA amends section 515(d) of the act to state that PMA supplements are required for all changes that affect safety or effectiveness, unless such change involves modifications in a manufacturing procedure or method of manufacturing. Clearance for this information collection, included within a proposed rule, has already been sought by FDA in an earlier document (63 FR 20558, April 27, 1998).

Section 205(c) of FDAMA amends section 515(d) of the act to allow for approval of incremental changes in design affecting safety and effectiveness based on nonclinical data that demonstrate the change creates the intended additional capacity, function, or performance of the device; and clinical data included in the original PMA application or any supplement to that application that provides reasonable assurance of safety and effectiveness. If needed, FDA may require a sponsor to submit new clinical data to demonstrate safety and effectiveness.

Section 207 of FDAMA amends section 513 of the act to allow an applicant who submits a premarket notification submission [510(k)] and receives a not substantially equivalent (NSE) determination, placing the device into a Class III category, to request FDA to classify the product into Class I or II. The request must be in writing and sent within 30 days from the receipt of the NSE determination. Within 60 days from the date the written request is submitted to FDA, the agency must classify the device by written order.

If FDA classifies the device into Class I or II, this device can be used as a predicate device for other 510(k)s. However, if FDA determines that the device will remain in Class III, the device cannot be distributed until the applicant has obtained an approved PMA or an approved investigational device exemption (IDE).

Section 208 of FDAMA amends section 513 of the act to allow PMA applicants to have the same access as FDA to data and information submitted by FDA to a classification panel, except data not available for public disclosure; the opportunity to submit information based on the PMA, through FDA, to the panel; and the same opportunity as FDA to participate in panel meetings.

Section 209(b) of FDAMA amends section 515(d) of the act to state that FDA must, upon the written request of the applicant, meet with that party within 100 days of receipt of the filed PMA application to discuss the review status of the application. With the concurrence of the applicant, a different schedule may be established. Prior to this meeting, FDA must inform the applicant in writing of any identified deficiencies and what information is required to correct those deficiencies. FDA must also promptly notify the applicant if FDA identifies additional deficiencies or of any additional information required to complete agency review.

FDA estimates the burden of this collection of information is as follows:

TABLE 1.—ESTIMATED ANNUAL REPORTING BURDEN¹

21 CFR Section	No. of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Hours
814.15, 814.20, and 814.37	52	1	52	837.28	43,539
814.82	37	1	37	134.68	4,983
814.84	37	1	37	10	370
Total					48,892

¹ There are no capital costs or operating and maintenance costs associated with this collection of information.

TABLE 2.—ESTIMATED ANNUAL RECORDKEEPING BURDEN¹

21 CFR Section	No. of Recordkeepers	Annual Frequency per Recordkeeping	Total Annual Records	Hours per Recordkeeper	Total Hours
814.82(a)(5) and (a)(6) Total	814	1	814	16.7	13,594 13,594

¹ There are no capital costs or operating and maintenance costs associated with this collection of information.

III. Reporting/Disclosure

The reporting burden can be broken out by certain sections of the PMA regulation.

§ 814.15—*Research conducted outside the United States*

§ 814.20—*Application*

§ 814.37—*PMA amendments and resubmitted PMA's*

The bulk of the burden is due to the previous three requirements. Included in these three requirements are the conduct of laboratory and clinical trials as well as the analysis, review, and physical preparation of the PMA application. FDA estimate of the hours per response (837.28) was derived through FDA's experience and consultation with industry and trade associations. Included in these three requirements are the conduct of laboratory and clinical trials as well as the analysis, review, and physical preparation of the PMA application. FDA estimates, based on the 1985 study, that these requirements account for the bulk of the burden identified by manufacturers.

IV. § 814.39—PMA Supplements

Clearance for this information collection, included within a proposed rule, has already been sought by FDA in an earlier document (63 FR 20558).

V. § 814.82—Postapproval Requirements

Postapproval requirements concern approved PMA's for devices that were not reclassified and require an annual report. In the last decade (1988 to 1997), the range of PMA's which fit this category averaged approximately 37 per year (70 percent of the 52 annual submissions). Most approved PMA's have been subject to some restriction. Approximately half of the average

submitted PMA's (26) require associated post approval information (i.e. clinical trials or additional preclinical information) that is labor-intensive to compile and complete, and the other PMA's require minimal information. Based on its experience and on consultation with industry, FDA estimates that preparation of reports and information required by this section requires 4,983 hours (134.68 hours per respondent).

VI. § 814.84

Postapproval requirements described in § 814.82 require a periodic report. FDA has determined respondents meeting the criteria of § 814.84 will submit reports on an annual basis. As stated previously, the range of PMA's fitting this category averaged approximately 37 per year. These reports have minimal information requirements. FDA estimates that respondents will construct their report and meet their requirements in approximately 10 hours. This estimate is based on FDA's experience and on consultation with industry. FDA estimates that the periodic reporting required by this section take 370 hours.

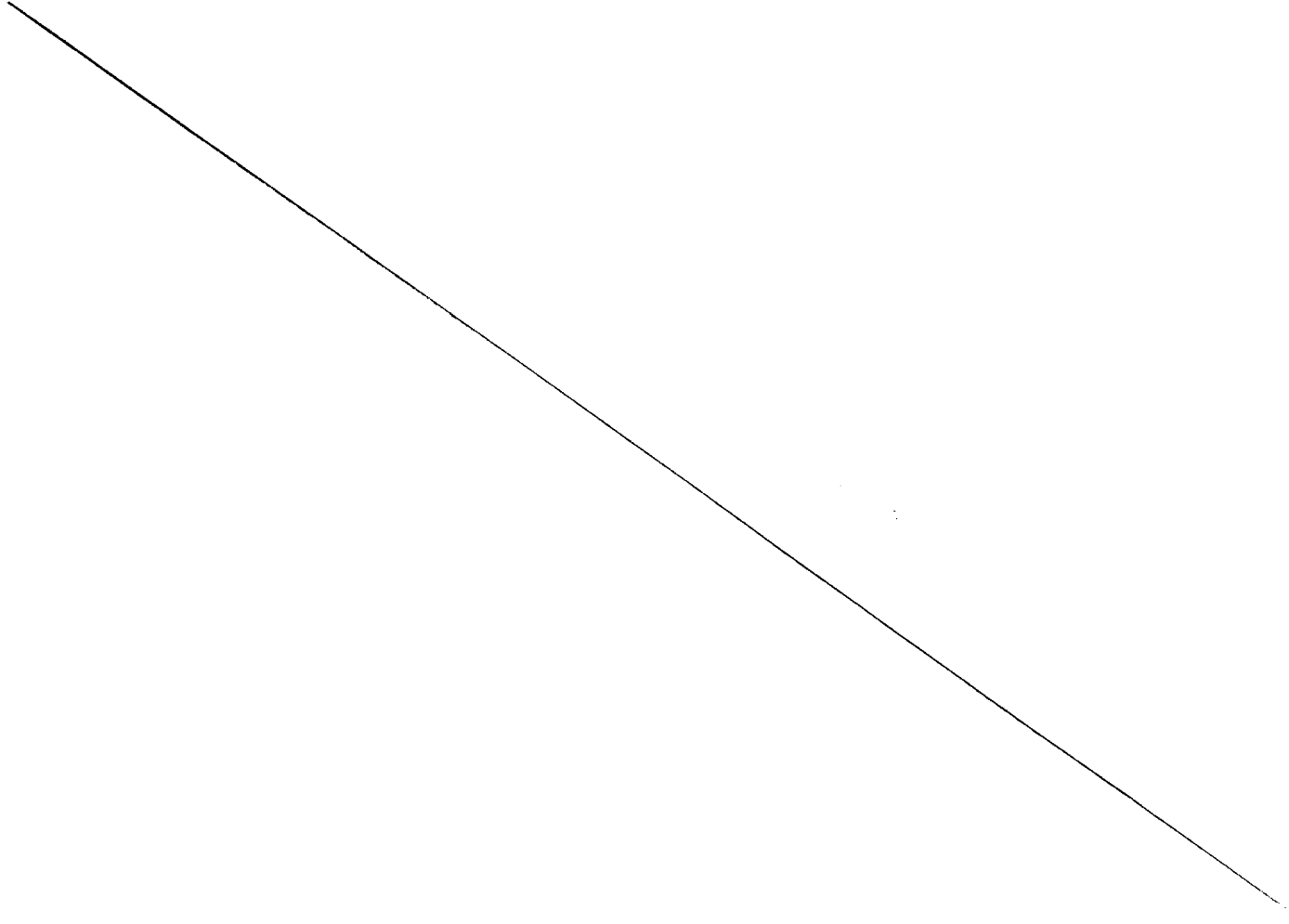
VII. Recordkeeping

The recordkeeping burden in this section involves the maintenance of records to trace patients and the organization and indexing of records into identifiable files to ensure the device's continued safety and effectiveness. These requirements are to be performed only by those manufacturers who have an approved PMA and who had original clinical research in support of that PMA. For a typical year's submissions, 70 percent of the PMA's are eventually approved and close to 100 percent of those have original clinical trial data. Therefore, about 37 PMA's a year (52 annual submissions times 70 percent) would be subject to these requirements. Also, because the requirements apply to all active PMA's, all holders of active PMA applications must maintain these records. PMA's have been required since 1976, so there are around 814 active PMA's that could be subject to these requirements (22 years x 37 per year). Each study has approximately 200 subjects, and, at an average of 5 minutes per subject, there is a total burden per study of

1,000 minutes, or 16.7 hours. The aggregate burden for all 814 holders of approved original PMA's, therefore, is 13,594 hours.

The applicant determines which records should be maintained during product development to document and/or substantiate the device's safety and effectiveness. Records required by the current good manufacturing practice (CGMP)/quality systems (QS) regulation (21 CFR part 820) may be relevant to a PMA review and may be submitted as part of an application. In individual instances, records may be required as conditions to approval to ensure the device's continuing safety and effectiveness.

Respondents to this information collection are persons filing an application with the Secretary of Health and Human Services for approval of a Class III medical device. Part 814 defines a person as any individual, partnership, corporation, association, scientific or academic



establishment, government agency or organizational unit, or other legal entity. These respondents include manufacturers of commercial medical devices in distribution prior to May 28, 1976 (the enactment date of the Medical Device Amendments).

Dated: September 28, 1998
September 28, 1998



William K. Hubbard
Associate Commissioner for Policy Coordination

[FR Doc. 98-???? Filed ??-??-98; 8:45 am]

BILLING CODE 4160-01-F

CERTIFIED TO BE A TRUE COPY OF THE ORIGINAL

